

(FILE 'HOME' ENTERED AT 19:04:23 ON 18 MAY 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
AT 19:04:41 ON 18 MAY 2003

L1 20031 S RETROVIR? VECTOR?
L2 289 S L1 AND ((SPLICE DONOR) OR (SPLICE ACCEPTOR) OR SA OR SD)
L3 150 DUP REM L2 (139 DUPLICATES REMOVED)
L4 49 S L3 AND PY<=1996
L5 49 FOCUS L4 1-
L6 13 S L4 AND DIFF?
L7 7425 S L1 AND (((SPLICE DONOR) OR (SPLICE ACCEPTOR) OR SA OR SD) (L)
L8 139 S L7 AND INTRON
L9 66 DUP REM L8 (73 DUPLICATES REMOVED)
L10 66 FOCUS L9 1-

=> d an ti so au ab pi 7 6 5

L10 ANSWER 7 OF 66 CAPLUS COPYRIGHT 2003 ACS

AN 1998:268635 CAPLUS

DN 128:291139

TI Construction of TRIN **retroviral vectors** contg.

Rev-responsive element of **HIV1** virus

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

IN Kingsman, Susan Mary; Kingsman, Alan John

AB **Retroviral vector** particles having an RNA genome carrying sequences which provide in the DNA provirus at least one selected gene located within an **intron** in a transcription unit of the provirus, which transcription unit further comprises a polynucleotide response element which is responsive to a nucleus to cytoplasm transport factor such as **HIV** Rev. These vectors have been named TRIN (Tat and Rev inducible) vectors. Expression of the selected genes is thus rendered Rev-dependent and so is dependent upon the presence of **HIV**. The TRIN vectors also contain the **murine** leukemia virus splice donor site, the strong CMV promoter, a packaging signal, and the **HIV** U5 and R regions.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9817817	A1	19980430	WO 1997-GB2859	19971017
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9747124	A1	19980515	AU 1997-47124	19971017
GB 2331989	A1	19990609	GB 1999-4143	19971017
GB 2331989	B2	20000927		
EP 931157	A1	19990728	EP 1997-909438	19971017
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2001502904	T2	20010306	JP 1998-519088	19971017
US 2002141978	A1	20021003	US 1999-254529	19990804

L10 ANSWER 6 OF 66 CAPLUS COPYRIGHT 2003 ACS

AN 2000:889060 CAPLUS

DN 135:71837

TI Use of **intron**-disrupted polyadenylation sites to enhance expression and safety of **retroviral vectors**

SO Journal of Virology (2001), 75(1), 199-204

CODEN: JOVIAM; ISSN: 0022-538X

AU Ismail, Said I.; Rohll, Jonathan B.; Kingsman, Susan M.; Kingsman, Alan J.; Uden, Mark

AB Normal mRNA polyadenylation signals are composed of an AAUAAA motif and G/U box spaced 20 to 30 bp apart. If this spacing is increased further, then polyadenylation is disrupted. Previously it has been demonstrated that insertion of an **intron** will similarly disrupt this signal even though such **introns** are removed during a nuclear splicing

reaction. This observation has led to the suggestion that polyadenylation site selection is undertaken prior to **intron** excision. We now present results that both support and extend these observations and in doing so create a novel class of retroviral expression vector with improved qualities. We found that when an **intron**-disrupted polyadenylation signal is inserted within a retroviral expression vector, such a signal, although reformed in the producer cell, remains benign until transduction, where it is then preferentially used. Thus, we demonstrate that upon transduction these vectors now produce a majority of shortened subgenomic species and as a consequence have a reduced tendency for subsequent mobilization from transduced cells. In addn., we demonstrate that the use of this internal signal leads to enhanced expression from such vectors and that this is achieved without any loss in titer. Therefore, split polyadenylation signals confer enhanced performance and improved safety upon retroviral expression vectors into which they are inserted. Such split signals may prove useful for the future optimization of **retroviral vectors** in gene therapy.

L10 ANSWER 5 OF 66 CAPLUS COPYRIGHT 2003 ACS

AN 1999:223066 CAPLUS

DN 130:247863

TI **Retroviral vectors** comprising functional splice donor and acceptor sites formed by reverse transcription of a pro-vector

SO PCT Int. Appl., 138 pp.

CODEN: PIXXD2

IN Bebbington, Chris; Kingsman, Susan; Uden, Mark; Kingsman, Alan; Mitrophanos, Kyriacos

AB A **retroviral vector** is claimed comprising a functional splice donor site and a functional splice acceptor site; wherein the functional splice donor site and the functional splice acceptor site flank a first nucleotide sequence of interest ("NOI"); wherein the functional splice donor site is upstream of the functional splice acceptor site; wherein the **retroviral vector** is derived from a retroviral pro-vector; wherein the retroviral pro-vector comprises a first nucleotide sequence ("NS") capable of yielding the functional splice donor site and a second NS capable of yielding the functional splice acceptor site; wherein the first NS is downstream of the second NS; such that the **retroviral vector** is formed as a result of reverse transcription of the retroviral pro-vector. This system for generating **retroviral vectors** is useful for transfection and gene therapy offers improved safety.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9915683	A1	19990401	WO 1998-GB2867	19980923
W:			AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
CA 2304259	AA	19990401	CA 1998-2304259	19980923
AU 9891756	A1	19990412	AU 1998-91756	19980923
AU 750110	B2	20020711		
GB 2344592	A1	20000614	GB 2000-6992	19980923
GB 2344592	B2	20020911		
EP 1017837	A1	20000712	EP 1998-944085	19980923
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO	
JP 2001517452	T2	20011009	JP 2000-512972	19980923
NZ 503317	A	20020531	NZ 1998-503317	19980923
NO 2000001486	A	20000525	NO 2000-1486	20000322

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RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9747124	A1	19980515	AU 1997-47124	19971017
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GB 2331989	B2	20000927		
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JP 2001502904	T2	20010306	JP 1998-519088	19971017
US 2002141978	A1	20021003	US 1999-254529	19990804

=>

Number	Hits	Search Text	DB	Time stamp
3	141	retrovir\$15 and (HIV WITH U3)	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/05/18 18:48
10	46	KINGSMAN-ALAN-JOHN	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/05/18 18:48
17	19	(vector SAME (TRIN or TIN)) and retrovir\$5	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/05/18 18:48
24	54	(retrovir\$15 and (HIV WITH U3 WITH R)) and REV	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/05/18 18:58
-	17718	retrovir\$15	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/07 10:28
-	58	retrovir\$15 and (HIV WITH U3 WITH R)	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/07 10:29
-	1	LISZIEWICZ-JULIANNA	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/07 11:25
-	2	LISZIEWICZ-J\$15	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/07 11:25
-	17718	retrovir\$15	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/08 14:04
-	7505	retrovir\$15 and (MULV or MLV or moMLV or murine or moloney)	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/08 14:05
-	5407	((retrovir\$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR))	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/08 18:43
-	2553	((retrovir\$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/08 14:06
-	1241	((retrovir\$15 and (MULV or MLV or moMLV or murine or moloney)) and (U3 or rre or rev or tat or LTR)) and (donor or acceptor)) and HIV	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/08 14:07
-	11722	(435/20.1).CCL3.	USPAT; US-EPUB; EPC; JPC; DEFWENT; USOCF	2002/03/08 14:08

-	702	vector SAME (TRIN or TIN)	USEFAT; US-PGPUE; EPC; JPC; DEFWENT; USOCP	2002/10/30 10:29
-	11	Retrovir\$5 and TRIN	USEFAT; US-PGPUE; EPC; JPC; DEFWENT; USOCP	2003/05/16 15:10